

CLAIM LISTING

Claims 1-47 (Cancelled)

48. (Currently Amended) An automated apparatus for forming an array of ligands on a support having localized areas, comprising:

~~a dispenser in fluid communication with a solution~~ one or more dispensers supplied with one or more solutions of a monomer or polymer,

wherein the dispenser is operative to dispense a volume of solution in a single coupling step of less than 5 nl at a distance away from a localized area,

a support having a surface and having a density of localized areas at least about 1000 localized areas per cm², and

a positioning system having a translational controller configured to repeatedly position the dispenser relative to ~~the~~ individual localized areas on the support in a manner to allow the dispenser to dispense the monomer or polymer for attachment at the individual localized areas until an array of at least 100 different ligands each at individual localized areas is formed ~~by the dispenser dispensing the solution of the monomer or polymer onto the support.~~

49. (Previously Prevented) The apparatus of claim 48 wherein the monomer or polymer is dissolved in the solution.

50. (Cancelled)

51. (Previously Presented) The apparatus of claim 48 wherein the dispenser is operative to contact the support.

52. (Previously Presented) The apparatus of claim 48 wherein the support further comprises a cover plate.

53. (Previously Presented) The apparatus of claim 48 wherein the positioning system is capable of positioning the dispenser between 5 microns and 50 microns away from the support.

54. (Previously Presented) The apparatus of claim 48 wherein the positioning system is capable of positioning the dispenser 10 microns away from the support.

55. (Previously Presented) The apparatus of claim 48 wherein the volume fits within a region on the support having a diameter of less than 300 microns.

56. (Cancelled)

57. (Previously Prevented) The apparatus of claim 48 wherein the monomer comprises a nucleotide or an amino acid.

58. (Previously Prevented) The apparatus of claim 48 wherein the polymer comprises a nucleic acid, oligonucleotide, polynucleotide, peptide, polypeptide, presynthesized polymer, polyurethane, polyester, polycarbonate, polyurea, polyamide, polyethyleneimine, polyacetate, receptor, enzyme, antibody, catalytic polypeptide, hormone receptor, or opiate receptor.

59. (Previously Prevented) The apparatus of claim 48 wherein the polymer comprises at least 2 monomers.

60. (Previously Prevented) The apparatus of claim 48 wherein the polymer comprises greater than 100 monomers.

61. (Previously Prevented) The apparatus of claim 48 wherein the polymer comprises at least 2, 3, 4, 5, 6, 10, 15, 20, 30, 40, 50, 75, or 100 monomers.

62. (Previously Presented) The apparatus of claim 48 wherein the support is selected from the group consisting of substantially flat substrates, substrates having raised or depressed regions, beads, gels, sheets, particles, strands, precipitates, spheres, containers, capillaries, pads, slices, films, plates, and slides.

63. (Previously Presented) The apparatus of claim 48 wherein the support comprises a gel.

64. (Previously Presented) The apparatus of claim 48 wherein the support comprises biological materials, nonbiological materials, organic materials or inorganic materials.

65. (Previously Presented) The apparatus of claim 48 wherein the support is a disc, square, or circle.

66. (Previously Presented) The apparatus of claim 48 wherein the localized area is smaller than 1mm^2 .

67. (Previously Presented) The apparatus of claim 48 wherein the localized area is smaller than 0.5mm^2 .

68. (Previously Presented) The apparatus of claim 48 wherein the localized area is smaller than $10,000\ \mu\text{m}^2$.

69. (Previously Presented) The apparatus of claim 48 wherein the localized area is smaller than $100\ \mu\text{m}^2$.

70. (Previously Presented) The apparatus of claim 48 wherein the array includes ligands that are at least 5% pure in their respective localized areas.

71. (Previously Presented) The apparatus of claim 48 wherein the array includes ligands that are at least between 10% and 20% pure in their respective localized areas.

72. (Previously Presented) The apparatus of claim 48 wherein the array includes ligands that are at least between 80% and 90% pure in their respective localized areas.

73. (Previously Presented) The apparatus of claim 48 wherein the array includes ligands that are at least greater than 95% pure in their respective localized areas.

74. (Cancelled)

75. (Previously Presented) The apparatus of claim 48 wherein the array includes at least 1000 different ligands at different localized areas.

76. (Previously Presented) The apparatus of claim 48 wherein the array includes at least 10,000 different ligands at different localized areas.

77. (Previously Presented) The apparatus of claim 48 wherein the array includes at least 100,000 different ligands at different localized areas.

78. (Previously Presented) The apparatus of claim 48 wherein the array includes at least 1,000,000 different ligands at different localized areas.

79. (Previously Presented) The apparatus of claim 48, wherein the array includes at least 1000 different ligands occupying localized areas within 1 cm² of the surface of the support.

80. (Previously Presented) The apparatus of claim 48, wherein the support comprises glass, derivatized glass, borosilicate glass, quartz, a polymeric material, polystyrene, polycarbonate, silicon or a gel.

81. (Previously Prevented) The apparatus of claim 48, wherein the solution of the monomer or polymer comprises an aqueous solution.

82. (Previously Presented) The apparatus of claim 48 wherein the apparatus includes a plurality of dispensers.

83. (Previously Presented) The apparatus of claim 48, wherein the support bears at least two reference points for positioning the dispenser over at least one of said localized areas for release of said volume of solution.

84. (Previously Presented) The apparatus of claim 83, wherein the reference points comprise global reference points for positioning the dispenser over a local region of the surface of the support, and local reference points within the local region for positioning the dispenser over a localized area within the local region.

85. (Previously Presented) The apparatus of claim 83, wherein the dispenser further comprises a camera for identifying the reference points.

86. (Previously Presented) The apparatus of claim 83 further comprising a device for sensing changes in capacitance to identify the reference points.

87. (Previously Presented) The apparatus of claim 83 further comprising a device for sensing changes in light intensity to identify the reference points.

88. (Previously Presented) The apparatus of claim 83 further comprising a device for sensing changes in resistivity to identify the reference points.

89. (Previously Presented) The apparatus of claim 83 further comprising a device for sensing changes in optical properties to identify the reference points.

90. (Previously Presented) The apparatus of claim 83 further comprising a device for sensing changes in magnetic properties to identify the reference points.

91. (Previously Presented) The apparatus of claim 82 wherein the plurality of dispensers comprises a manifold of delivery lines.

92. (Previously Presented) The apparatus of claim 82 wherein the plurality of dispensers comprises an array of pipettes.

93. (Previously Presented) The apparatus of claim 82 wherein the plurality of dispensers comprises a series of tubes.

94. (Previously Presented) The apparatus of claim 82 wherein the plurality of dispensers includes control valves.

95. (Previously Presented) The apparatus of claim 48 wherein the support includes linker molecules.

96. (Previously Presented) The apparatus of claim 48 wherein the dispenser is moveable relative to the support.

97. (Previously Presented) The apparatus of claim 48 wherein the support is moveable relative to the dispenser.

98. (Previously Presented) The apparatus of claim 48 wherein the one or more localized areas are spaced less than 3 mm apart.

99. (Previously Presented) The apparatus of claim 48 wherein the one or more localized areas are spaced less than between 5 microns and 100 microns apart.

100. (Previously Presented) The apparatus of claim 48 wherein the one or more localized areas has an angular relation between each localized area of about 1 degree.

101. (Previously Presented) The apparatus of claim 48 wherein the one or more localized areas has an angular relation between each localized area of about 0.1 degree.

102. (Previously Presented) The apparatus of claim 48 wherein the support comprises at least 100 localized areas.

103. (Previously Presented) The apparatus of claim 48 wherein the support comprises at least 1000 localized areas.

104. (Previously Presented) The apparatus of claim 48 wherein the support comprises at least 10,000 localized areas.

105. (Cancelled)

106. (Previously Presented) The apparatus of claim 48 wherein the support comprises at least 10,000 localized areas per cm^2 of surface of substrate.

107. (Previously Presented) The apparatus of claim 48 wherein the support comprises a strand including one or more of glass, derivatized glass, quartz, or a polymeric material.

108. (Previously Presented) The apparatus of claim 48 wherein the dispenser comprises a dispenser tip and a sheath encircling the dispenser tip and rigidly extending a fixed distance beyond the dispenser tip.

109. (Previously Presented) The apparatus of claim 48 wherein the surface of the support comprises a hydrophilic or hydrophobic substance.

110. (Previously Presented) The apparatus of claim 48 wherein the surface of the support comprises a photoresist.

111. (Previously Presented) The apparatus of claim 48 wherein the surface of the support is pretreated.

112. (Previously Presented) The apparatus of claim 48 wherein the dispenser comprises a pipette.

113. (Previously Presented) The apparatus of claim 48 wherein the dispenser comprises a capillary tube.

114. (Previously Presented) The apparatus of claim 48 wherein the dispenser comprises an osmotic pump.

115. (Previously Presented) The apparatus of claim 48 wherein the dispenser comprises a cell sorter.

116. (Previously Presented) The apparatus of claim 48, wherein the array includes at least 10,000 different polymers occupying localized areas within 1 cm^2 of the surface of the support.

117. (Previously Presented) The apparatus of claim 48 wherein the dispenser and the substrate have a common frame of reference.

118. (Previously Presented) The apparatus of claim 48 wherein the dispenser is coupled to a translational mechanism.

119. (Previously Presented) The apparatus of claim 118 wherein the translational mechanism moves at a rate of 3 to 10 stops per second.

120. (Previously Presented) The apparatus of claim 119 wherein the translational mechanism is accurate within $1 \text{ }\mu\text{m}$.

121. (Previously Presented) The apparatus of claim 118 wherein the translational mechanism includes a closed loop position feedback mechanism.

122. (Previously Presented) The apparatus of claim 118 wherein the translational mechanism operates with insignificant backlash.

123. (Previously Presented) The apparatus of claim 118 wherein the translational mechanism is an electro-mechanical mechanism.

124. (Previously Presented) The apparatus of claim 123 wherein the electro-mechanical mechanism has a greater than 1 μm repeatability relative to reaction region diameter travel distance.

125. (Previously Presented) The apparatus of claim 48 wherein the dispenser is operative to repeatedly perform single coupling steps wherein each coupling step dispenses droplets no greater than 5 nl to the same or a different localized area.

126. (Previously Presented) The apparatus of claim 83 including a laser for locating a reference point.

Claims 127-151 (Cancelled)

152. (Currently Amended) An automated apparatus for forming an array of ligands on a support having localized areas, comprising:

~~a dispenser comprising an array of dispensing units in fluid communication with a solution~~ supplied with one or more solutions of a monomer or polymer,

wherein the dispensing units are operative to dispense droplets in a single coupling step of no greater than 5 nl at a distance away from a localized area,

a support having a surface and having a density of localized areas at least about 1000 localized areas per cm^2 , and

a positioning system including a translational controller capable of repeatedly positioning the dispensing units ~~dispenser~~ relative to individual localized areas on the support in a manner to allow the dispensing units to dispense the monomer or polymer for attachment at the

individual localized areas until an array of at least 100 different ligands each at individual localized areas is formed ~~by the dispenser dispensing the solution of the monomer or polymer onto the support.~~

153. (Cancelled)

154. (Previously Prevented) The apparatus of claim 152 wherein the monomer or polymer is dissolved in the solution.

155. (Previously Presented) The apparatus of claim 152 wherein the dispenser is operative to contact the support.

156. (Previously Presented) The apparatus of claim 152 wherein the droplet fits within a region on the support having a diameter of less than 300 microns.

157. (Cancelled)

158. (Previously Prevented) The apparatus of claim 152 wherein the monomer comprises a nucleotide or an amino acid.

159. (Previously Prevented) The apparatus of claim 152 wherein the polymer comprises a nucleic acid, oligonucleotide, polynucleotide, peptide, polypeptide, presynthesized polymer, polyurethane, polyester, polycarbonate, polyurea, polyamide, polyethyleneimine, polyacetate, receptor, enzyme, antibody, catalytic polypeptide, hormone receptor, or opiate receptor.

160. (Previously Prevented) The apparatus of claim 152 wherein the polymer comprises at least 2 monomers.

161. (Previously Prevented) The apparatus of claim 152 wherein the polymer comprises greater than 100 monomers.

162. (Previously Prevented) The apparatus of claim 152 wherein the polymer comprises 2, 3, 4, 5, 6, 10, 15, 20, 30, 40, 50, 75, or 100 monomers.

163. (Previously Presented) The apparatus of claim 152 wherein the support is selected from the group consisting of substantially flat substrates, substrates having raised or depressed regions, beads, gels, sheets, particles, strands, precipitates, spheres, containers, capillaries, pads, slices, films, plates, and slides.

164. (Previously Presented) The apparatus of claim 152 wherein the support comprises a gel.

165. (Previously Presented) The apparatus of claim 152 wherein the support comprises biological materials, nonbiological materials, organic materials or inorganic materials.

166. (Previously Presented) The apparatus of claim 152 wherein the support is a disc, square, or circle.

167. (Previously Presented) The apparatus of claim 152 wherein the localized area is smaller than 1mm^2 .

168. (Previously Presented) The apparatus of claim 152 wherein the localized area is smaller than 0.5mm^2 .

169. (Previously Presented) The apparatus of claim 152 wherein the localized area is smaller than $10,000\text{ }\mu\text{m}^2$.

170. (Previously Presented) The apparatus of claim 152 wherein the localized area is smaller than $100\text{ }\mu\text{m}^2$.

171. (Previously Presented) The apparatus of claim 152 wherein the array of substances includes at least 100 different polymers at different localized areas.

172. (Currently Amended) The apparatus of claim 152 wherein the array of ligands ~~substances~~ includes at least 1000 different polymers at different localized areas.

173. (Currently Amended) The apparatus of claim 153 wherein the array of ligands ~~substances~~ includes at least 10,000 different polymers at different localized areas.

174. (Currently Amended) The apparatus of claim 154 wherein the array of ligands ~~substances~~ includes at least 100,000 different polymers at different localized areas.

175. (Currently Amended) The apparatus of claim 155 wherein the array of ligands ~~substances~~ includes at least 1,000,000 different polymers at different localized areas.

176. (Currently Amended) The apparatus of claim 152, wherein the array of ligands ~~substances~~ includes at least 1000 different polymers occupying localized areas within 1 cm² of the surface of the support.

177. (Previously Presented) The apparatus of claim 152, wherein the support comprises glass, derivatized glass, borosilicate glass, quartz, a polymeric material, polystyrene, polycarbonate, silicon or a gel.

178. (Previously Presented) The apparatus of claim 152, wherein the solution comprises an aqueous solution.

179. (Previously Presented) The apparatus of claim 152, wherein the support bears at least two reference points for positioning the dispenser over at least one of said localized areas for release of said droplet.

180. (Previously Presented) The apparatus of claim 179, wherein the reference points comprise global reference points for positioning the dispenser over a local region of the surface of the support, and local reference points within the local region for positioning the dispenser over a localized area within the local region.

181. (Previously Presented) The apparatus of claim 179, wherein the dispenser further comprises a camera for identifying the reference points.

182. (Previously Presented) The apparatus of claim 179 further comprising a device for sensing changes in capacitance to identify the reference points.

183. (Previously Presented) The apparatus of claim 179 further comprising a device for sensing changes in light intensity to identify the reference points.

184. (Previously Presented) The apparatus of claim 179 further comprising a device for sensing changes in resistivity to identify the reference points.

185. (Previously Presented) The apparatus of claim 179 further comprising a device for sensing changes in optical properties to identify the reference points.

186. (Previously Presented) The apparatus of claim 179 further comprising a device for sensing changes in magnetic properties to identify the reference points.

187. (Previously Presented) The apparatus of claim 152 wherein the array of dispensing units comprises a manifold of delivery lines.

188. (Previously Presented) The apparatus of claim 152 wherein the array of dispensing units comprises an array of pipettes.

189. (Previously Presented) The apparatus of claim 152 wherein the array of dispensing units comprises a series of tubes.

190. (Currently Amended) The apparatus of claim 152 wherein the array of dispensing units ~~dispenser~~ is moveable relative to the support.

191. (Currently Amended) The apparatus of claim 152 wherein the support is moveable relative to the array of dispensing units ~~dispenser~~.

192. (Previously Presented) The apparatus of claim 152 wherein the one or more localized areas are spaced less than 3 mm apart.

193. (Previously Presented) The apparatus of claim 152 wherein the one or more localized areas are spaced less than between 5 microns and 100 microns apart.

194. (Previously Presented) The apparatus of claim 152 wherein the one or more localized areas has an angular relation between each localized area of about 1 degree.

195. (Previously Presented) The apparatus of claim 152 wherein the one or more localized areas has an angular relation between each localized area of about 0.1 degree.

196. (Previously Presented) The apparatus of claim 152 wherein the support comprises at least 100 localized areas.

197. (Previously Presented) The apparatus of claim 152 wherein the support comprises at least 1000 localized areas.

198. (Previously Presented) The apparatus of claim 152 wherein the support comprises at least 10,000 localized areas.

199. (Cancelled)

200. (Previously Presented) The apparatus of claim 152 wherein the support comprises at least 10,000 localized areas per cm^2 of surface of substrate.

201. (Previously Presented) The apparatus of claim 152 wherein the support comprises a strand including one or more of glass, derivatized glass, quartz, or a polymeric material.

202. (Previously Presented) The apparatus of claim 152 wherein the surface of the support comprises a hydrophilic or hydrophobic substance.

203. (Previously Presented) The apparatus of claim 152 wherein the surface of the support comprises a photoresist.

204. (Previously Presented) The apparatus of claim 152 wherein the surface of the support is pretreated.

205. (Previously Presented) The apparatus of claim 152, wherein the array of substances includes at least 10,000 different polymers occupying localized areas within 1 cm^2 of the surface of the support.

206. (Previously Presented) The apparatus of claim 152 including a laser for locating a reference point.

207. (Currently Amended) An automated apparatus for forming an array of polypeptides or polynucleotides on a support having localized areas, comprising:

~~a dispenser in fluid communication with a solution~~ one or more dispensers supplied with plural solutions of polypeptides or polynucleotides,

wherein the dispenser is operative to dispense a volume of the solution in a single coupling step of less than 5 nl at a distance away from a localized area,

a support having a density of localized areas at least about 1000 localized areas per cm²,
and

a positioning system including a translation controller configured to repeatedly position the dispenser relative to the individual localized areas on the support in a manner to allow the dispenser to dispense the polypeptides or polynucleotides for attachment at the individual localized areas until an array of at least 1000 different ligands each at individual localized areas is formed, ~~by the dispenser dispensing the solution of the polypeptides or polynucleotides onto the support.~~

208. (Previously Presented) The apparatus of claim 207 wherein the dispenser is operative to contact the support.

209. (Previously Presented) The apparatus of claim 207 wherein the positioning system is capable of positioning the dispenser between 5 microns and 50 microns away from the support.

210. (Previously Presented) The apparatus of claim 207 wherein the volume fits within a region on the support having a diameter of less than 300 microns.

211. (Previously Presented) The apparatus of claim 207 wherein the polypeptide or polynucleotide comprises at least 2, 3, 4, 5, 6, 10, 15, 20, 30, 40, 50, 75, or 100 monomers.

212. (Previously Presented) The apparatus of claim 207 wherein the support is selected from the group consisting of substantially flat substrates, substrates having raised or depressed regions, beads, gels, sheets, particles, strands, precipitates, spheres, containers, capillaries, pads, slices, films, plates, and slides.

213. (Previously Presented) The apparatus of claim 207 wherein the support comprises a gel.

214. (Previously Presented) The apparatus of claim 207 wherein the localized area is smaller than 0.5mm^2 .

215. (Previously Presented) The apparatus of claim 207 wherein the localized area is smaller than $10,000\text{ }\mu\text{m}^2$.

216. (Previously Presented) The apparatus of claim 207 wherein the apparatus includes a plurality of dispensers.

217. (Previously Presented) The apparatus of claim 216 wherein the plurality of dispensers comprises a manifold of delivery lines.

218. (Previously Presented) The apparatus of claim 216 wherein the plurality of dispensers comprises an array of pipettes.

219. (Previously Presented) The apparatus of claim 216 wherein the plurality of dispensers comprises a series of tubes.